REMARKS

The specification has been amended to set forth the status of the parent application and to amend the description of the Figure 7 in light of the formal drawings being submitted herewith. Claim 23 has been canceled as being drawn to a non-elected species. Claims 3, 4, 9, 14 and 19 have been canceled. The claims have been amended to refer to a "monocot" nucleic acid and to replace "gene" with "nucleic acid" to provide consistent use of the terms and antecedent basis in the claims. Claim 1 has further been amended to specify the modification. Claim 22 has been amended to specify the species of *Fusarium* as found on page 2, lines 3-10. It is submitted that none of these amendments constitute new matter and their entry is requested.

The Examiner objected to the Declaration as being defective with respect to claiming priority under 35 U.S.C. §120 to the parent application and with respect to the application being a continuation-in-part. It is submitted that the Examiner is in error in this objection. First, Applicants note that the Declaration uses the format prepared and furnished by the U.S. Patent and Trademark Office (PTO). This PTO-approved Declaration properly makes reference to duty of disclosure for a continuation-in-part application in the fifth paragraph where duty of disclosure is stated. This PTO-approved Declaration also does not make reference to any parent application under 35 U.S.C. §120, since this reference is made in the first paragraph of the specification as provided for by 37 C.F.R. §1.78. Thus, it is submitted that the Declaration is not defective and withdrawal of this rejection is requested.

With respect to the Examiner's comments concerning the Information Disclosure Statement. Applicants note that U.S. Patent No. 5,498,431 is equivalent to German patent application 4108746.

In response to the objection to the drawings, Applicants submit herewith formal drawings for Figures 7A-7F, 8A-8B and 9.

Applicants note that Examiner's objection to claims 6, 11 and 16. However, Applicants believe that this objection is improper at this time in view of the pendency of a generic claim and the appropriate inclusion of all of the subject matter of these claims should the generic claim be allowed.

The Examiner rejected claims 1-22 under 35 U.S.C. §112, second paragraph, for being indefinite. It is believed that the amendments and the remarks which follow obviate this rejection.

Specifically, Applicants have adopted the claim language as issued in their previous U.S. Patent No. 6,060,646, which has already been determined to be definite by the USPTO.

The Examiner has objected to the phrases "the modification is sufficient to reduce" and "is insufficient to destroy." Applicants respectfully traverse the Examiner's objection. This language was the language used in the parent application and thus, for consistency, and since it has been determined to be definite, Applicants are continuing to use this language. The Examiner's attention is directed to page 7 of the specification, where it describes that it is believed that the mycotoxin binds to the wild type protein, but not to the mutant gene product. Thus, the modified ribosomal L3 protein encoded by the modified nucleic acid of the present invention would still have to function as a peptidyl transferase in the ribosomal complex, but it would be modified to a sufficient extent to reduce the mycotoxin binding properties. If the mycotoxin has a reduced effect, the plant is more able to defend itself against the fungus, and thus reduce the incidence of disease. However, as noted above, the modified gene must still function to encode an active peptidyl transferase.

With respect to the Examiner's objection to Claims 1, 2, 3, 5, 10 and 15, regarding the use of the term "gene", this term has been replaced with the term "nucleic acid" in all cases. Applicants have also replaced the phrase "ribosomal protein L3" with the phrase "ribosomal L3 protein."

Applicants traverse the Examiner's objection to the phrase "a functional equivalent thereof" as used in Claims 6, 11 and 16. Again, this phrase was accepted in the parent application and for consistency, and since it has been determined to be definite, Applicants are maintaining use of this phrase in the present application.

Applicants have amended claim 7 to refer to the modified "monocot" nucleic acid to obviate the Examiner's objection.

Applicants traverse the Examiner's objection to Claim 22 for use of the term "a suitable plant". Again, this term was used and accepted in the parent application and for consistency, and since it has been determined to be definite, Applicants are maintaining use of this phrase in the present application.

In view of the amendments to the claims and the above remarks, it is submitted that the claims are definite, and particularly point out and distinctly claim the subject matter of the invention as required by 35 U.S.C. §112, second paragraph. Withdrawal of this rejection is requested.

The Examiner rejected claims 1-22 under 35 U.S.C. §112, first paragraph, for lack of written description. The Examiner contends that Applicants only described a modified rice gene and did not describe any other modified monocot genes. The Examiner further contends that Applicants did not describe any modifications other than that shown. Applicants traverse this rejection, especially in view of the amendments made to the claims.

Applicants submit that the amendments made to the claims address most of the issues raised by the Examiner under this rejection. The Claims as amended are now limited to a modification of a monocot nucleic acid at position 258, based on the rice numbering system, wherein the modification is sufficient to reduce the mycotoxin binding capabilities of the encoded ribosomal L3 protein, but is insufficient to destroy the function of the nucleic acid as a ribosomal protein nucleic acid. The language of the amended claims mirrors the language in the issued claims from Applicants' Patent 6,060,646, except the claim is directed to a modified monocot nucleic acid, whereas in the prior Patent, the claim was not so restricted. Claim 2 of US 6,060,646, being selected from the group consisting of rice, *Arabidopsis thalicina*, rat, mice, human and *C. elegans*. The present application includes additional data, beginning at Example 8, which supports the claim to the monocots, and shows the sequence of six different monocots and specifically, the sequence homology. As shown in Figure 8, the overall amino acid sequence identity is at least 92.5% with an identical alignment between amino acid 209 and 284 (based on the rice amino acid numbering system). Thus, Applicant respectfully submits that, despite the fact that the specification examples only provide an example with a modified rice, one of ordinary skill in the art, when reviewing the application (specifically Example 8 and the generic disclosure of modified gene encoding a modified peptide having the specified modification) readily realizes that due to the sequence homology, a similar modification made to position 258 in any of the monocot sequences disclosed in the application resulting in the same modification, (i.e., a modification which is sufficient to reduce the mycotoxin binding capabilities of the encoded ribosomal L3 protein but insufficient to destroy the function of the encoded protein as a ribosomal L3 protein) was contemplated by Applicants. Therefore, Applicants respectfully submit that the claims, as now amended, are adequately supported by the specification in full, clear, concise and exact terms, to indicate that Applicants were in possession of the invention as claimed. In view of these remarks, it is submitted that the claimed

invention complies with the written description requirement of 35 U.S.C. §112, first paragraph. Thus, withdrawal of this rejection is requested.

The Examiner rejected claims 1-22 under 35 U.S.C. §112, first paragraph, for lack of enablement. The Examiner contends that the specification is not enabling for any mutation in the gene encoding the ribosomal L3 protein. Furthermore, Applicant respectfully submits that a person of ordinary skill in the art would be able to prepare amino acid substitutions other than the Tryptophan to Cysteine substitution at the specified residue, such as by the well-known technique of site-directed mutagenesis. The skilled artisan would also be able to select modified genes that produce modified ribosomal L3 proteins that continue to function in the presence of the mycotoxin deoxynivalenol (DON) and thus, the modification is sufficient to reduce the mycotoxin binding capabilities of the encoded ribosome L3 protein, but insufficient to destroy its function as a ribosomal protein.

Furthermore, Applicants have identified two additional yeast strains, which grew well, both in the absence and presence of the mycotoxin DON. Both of these strains were using an Rpl3 gene that encodes the amino acid Arginine at position 255. Both of these strains have different DNA sequence in this region, that is to say, two separate codons for Arginine are being used by the two yeast Rpl3 genes. The yeast strains appear to grow in DON mycotoxin levels that are toxic or inhibitory to the wild-type strain and they grew as well as the strain with the cysteine at position 255. Therefore, Applicants respectfully submit that a person of ordinary skill in the art would be able to prepare amino acid substitutions other than the Tryptophan to Cysteine substitution and select modified genes which can continue to function in the presence of the mycotoxin DON and thus, the modification is sufficient to reduce the mycotoxin binding capabilities of the encoded ribosome L3 protein, but insufficient to destroy the protein as a ribosomal L3 protein. Thus, Applicants submit that requesting that Applicants limit their claims to the specific modification exemplified in the present application would amount to an invitation for potential infringers to practice Applicants' invention without infringing their claims.

In view of the amendments to the claims and these remarks, it is submitted that the claims are fully enabled by the specification. Withdrawal of this rejection is requested.

The Examiner rejected claims 1-21 under 35 U.S.C. §103(a) as being obvious over Kim et al. (1990) in view of Schultz et al. (1983) and further in view of Kim (1991) and Bohn et al. (1997). It is submitted that the amended claims obviate this rejection.

Kim et al (1990) describes two plant Rpl3 genes from the dicot plant *Arabidopsis thaliana*. This paper also refers to the work of Fried and Warner (1981), who discovered that the yeast mutant tcm1 gene confers tolerance of trichodermin in yeast. In Kim et al., Figure 3, on page 180, contains a comparison between the ARP1, ARP2 and TCM1 proteins. The Figure 3 legend clarifies that the TCM1 sequence is derived from the yeast tcm1 gene which is the mutant form of the Tcm1 gene. Page 180 of the D1 paper includes a discussion of the comparison of these three proteins, revealing the overall sequence identity and two highly conserved (but not identical) regions between residues 48-131 and 213-287. The critical sequence change between the wild-type yeast Tcm1 gene and the mutant yeast tcm1 gene was not known or revealed by Kim et al. in 1990.

Schultz teaches a *Saccharomyces cerevisiae* modified nucleic acid. However, prior to the present invention, there was no demonstration that the modification of a ribosomal L3 protein would function in plants. The expression/production of ribosomal genes/proteins and ribosome assembly in mammals and lower eukaryotes such as yeast has been shown to be stringently regulated e.g. rapid degradation of excess protein. Much less is known about how ribosomal genes and proteins are regulated and assembled in plants. There is no prior research demonstrating that one can modify a ribosomal protein gene, reintroduce it into a plant with a constitutive promoter, and have it function properly. Applicants demonstrated by tobacco transformation that the modified Rpl3 gene functioned in plants. This necessitated conducting site-specific mutagenesis on the rice Rpl3 cDNA, inserting the sequence into an *Agrobacterium* vector, and transforming tobacco plants. Since tobacco is not a host of *Fusarium graminearum*, Applicants needed to develop assays to test the direct effect of trichothecene mycotoxins on transformed tobacco cells and did so with cell suspension cultures as well as protoplasts. It was not sufficient to introduce the unmodified version of the rice Rpl3 gene — this did not confer any DON tolerance to the transgenic plant cells and protoplasts - it was the modification which was important to provide trichothecene tolerance. It could not be easily predicted that one could use information from a chemical tolerance mutant screen in yeast to produce a transgenic plant tolerant of a broad host fungal pathogen.

Kim (1991) is an abstract from a Ph.D. thesis. This abstract suggests that eight trichodermin-resistant mutant plants of *Arabidopsis thaliana* were isolated. There is, however, no genetic information provided in this abstract to suggest what modification of the *Arabidopsis* gene resulted in the mycotoxin resistance phenotype. Therefore, there is nothing in this abstract which would provide a person of ordinary skill in the art the present invention or make obvious the present invention.

The Bohn et al. reference (1997) in Genbank reveals that the wild-type tcm1 gene sequence was publically released on August 11, 1997, one day before the US parent application was filed. Even if one knew which amino acid had been altered in the yeast tcm1 coding sequence, it was also not obvious that the same modification in the plant RPL3 protein would function properly in plants. The protein RPL3 is one of ~70 plant ribosomal proteins. How these proteins are assembled, how they interact with each other and with ribosomal RNA, and what residues are essential for ribosomal activity are not known in plants and certainly cannot be predicted from the sequence data in Kim et al (1990) or what was known prior to Applicants' patent filing. The critical modification is within a highly conserved region and it is not obvious that, if one makes a change in this region, the protein can still function properly within the plant ribosomal complex.

Thus, it is respectfully submitted that the claims, as now amended, are patentable over Kim et al. (1990) in view of Schultz et al. (1983), Kim (1991) and Bohn et al. (1997). Withdrawal of this rejection is requested.

The Examiner rejected claim 22 under 35 U.S.C. §103(a) as being obvious over Fluhr et al. (1996) in view of Kim et al. (1990) and Schultz et al. (1983) and further in view of Kim (1991) and Bohn et al. (1997). It is submitted that the amended claim obviates this rejection.

Specifically, Applicants have amended claim 22 to specify that the resistance is to an infection by a *Fusarium* species selected from the group consisting of *F. graminearum, F. sambucinum, F. poae, F. sporotrichioides, F. culmorum* and *F. crookwellense*. Fluhr refers to resistance to *F. oxysporum*, a distantly related *Fusarium* with a very different infection process and causing wilt using a species/race-specific resistance mechanism that is completely unrelated to the resistance mechanism of the present invention. Thus, as now amended, Applicants respectfully

submit that claim 22 is not obvious over Fluhr et al., in view of Kim et al. (1990), Schultz et al. (1983), and further in view of Kim (1991) and Bohn et al. (1997), for this reason and the reasons previously discussed. Withdrawal of this rejection is requested.

Applicants note the Examiner's rejection of claims 1-22 under the judicially created doctrine of obviousness-type double patenting over claims 1-18 of U.S. Patent No. 6,060,646. Applicants also note the Examiner's rejection of claims 6, 11 and 16 under 35 U.S.C. §101 for double patenting over claims 4, 8 and 12 of U.S. Patent No. 6,060,646. Applicants intend to address these rejections once otherwise allowable subject matter is indicated by the Examiner. If the amended claims are otherwise allowable, the Examiner is invited to telephone the undersigned to expedite response to these rejections.

In view of the above amendments and remarks, it is believed that the present claims satisfy the provisions of the patent statutes and are patentable over the cited prior art. Reconsideration of the application and early notice of allowance are requested. The Examiner is invited to telephone the undersigned to expedite the prosecution of the application.

RESPECTFULLY SUBMITTED,			
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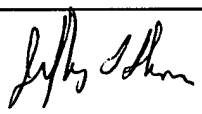
Signature		*Date*	27 January 2003

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Attachment: Marked-up Copy of Amendments

Marked-Up Copy of Amended Specification - Page 1, lines 4-6

The present application is a continuation-in-part application of U.S. patent application Serial No. 09/567,326 filed on May 9, 2000, now abandoned, which in turn is a continuation application of U.S. patent application Serial No. 08/909,828, filed on August 12, 1997, now U.S. patent No. 6,060,646.

Marked-Up Copy of Amended Specification - Page 6, lines 12-14

FIGURES 7A-7F [7H] show the alignment of nonocot *Rpl3* cDNA clones. The consensus sequences are aligned beginning at the putative ATG translation initiation codon, with the exception of the oat sequence which is a partial sequence.

Marked-Up Copy of Amended Claims

1 (amended). A modified monocot nucleic acid, wherein the wild type form of said monocot nucleic acid encodes a ribosomal L3 protein [L3] and wherein a host transformed with said modified nucleic acid is resistant to trichothecene mycotoxins, wherein the modification is sufficient to reduce the mycotoxin binding capabilities of the encoded ribosomal L3 protein [L3] but is insufficient to destroy the function of the [nucleic acid] encoded protein as a ribosomal L3 protein [gene], [with the proviso that said gene is not from *Saccharomyces cerevisiae*] wherein the modification is a single amino acid substitution for Trp at position 258 (based on the amino acid numbering of the rice nucleic acid).

2 (amended). The modified nucleic acid of claim 1, wherein the [gene] nucleic acid is modified by a base pair substitution, deletion, addition or inversion.

5 (amended). The modified nucleic acid of claim [4] 1, wherein the monocot nucleic acid encoding the ribosomal L3 protein [L3] nucleic acid is selected from the group consisting of: a rice nucleic acid, a corn [gene] nucleic acid, a sorghum [gene] nucleic acid, a wheat [gene] nucleic acid, a barley [gene] nucleic acid and an oat [gene] nucleic acid.

6 (amended). The modified nucleic acid of claim 5, wherein the nucleic acid has a sequence which will encode the amino acid sequence selected from the group consisting of SEQ ID [No.] NO:3, SEQ ID [No.] NO:14, SEQ ID [No.] NO:15, SEQ ID [No.] NO:16, SEQ ID [No.] NO:17 and SEQ ID [No.] NO:18, with the sequence encoding a cysteine at position 258, or a functional equivalent thereof.

7 (amended). A cloning vector containing [a] the modified [ribosomal protein L3] monocot nucleic acid as defined in claim 1.

10 (amended). The cloning vector of claim [9] 8, wherein the monocot nucleic acid encoding the ribosomal L3 protein [L3] is selected from the group consisting of: a rice nucleic acid, a corn [gene] nucleic acid, a wheat [gene] nucleic acid, a barley [gene] nucleic acid, and an oat [gene] nucleic acid.

11 (amended). The cloning vector of claim 10, wherein the nucleic acid has a sequence which will encode the amino acid sequence selected from the group consisting of SEQ ID [No.] NO:3, SEQ ID [No.] NO:14, SEQ ID [No.] NO:15, SEQ ID [No.] NO:16, SEQ ID [No.] NO:17 and SEQ ID [No.] NO:18, with the sequence encoding a cysteine at position 258, or a functional equivalent thereof.

12 (amended). A transformed plant transformed with [a] the modified [ribosomal protein L3] monocot nucleic acid of claim 1, wherein said transformed plant is resistant to infection by *Fusarium* [infestation] species which produce trichothecene mycotoxins.

15 (amended). The plant of claim [14] 13, wherein the nucleic acid encoding the ribosomal L3 protein [L3] is selected from the group consisting of a rice nucleic acid, a corn [gene] nucleic acid, a sorghum [gene] nucleic acid, a wheat [gene] nucleic acid, a barley [gene] nucleic acid and an oat [gene] nucleic acid.

16 (amended). The plant of claim 15, wherein the nucleic acid has a sequence which will encode the amino acid sequence selected from the group consisting of SEQ ID [No.] NO:3, SEQ ID [No.] NO:14, SEQ ID [No.] NO:15, SEQ ID [No.] NO:16, SEQ ID [No.] NO:17 and SEQ ID [No.] NO:18, with the sequence encoding a cysteine at position 258, or a functional equivalent thereof.

22 (amended). A method of increasing resistance to *Fusarium* species infestation by transforming a suitable plant with [a] the modified nucleic acid as defined in claim 1, wherein the

plant transformed with said nucleic acid [is resistant] has increased resistance to trichothecene mycotoxins and wherein said method comprises the steps of:

providing a modified nucleic acid and

transforming a suitable plant with said nucleic acid;

wherein the *Fusarium* species is selected from the group consisting of *F. graminearum, F. sambucinum, F. poae, F. sporotrichioides, F. culmorum* and *F. crookwellense*.